

FIGURE 1

cis/trans isomerization of a peptidyl-prolyl bond  
(Acetyl-prolyl-N-methylamid)

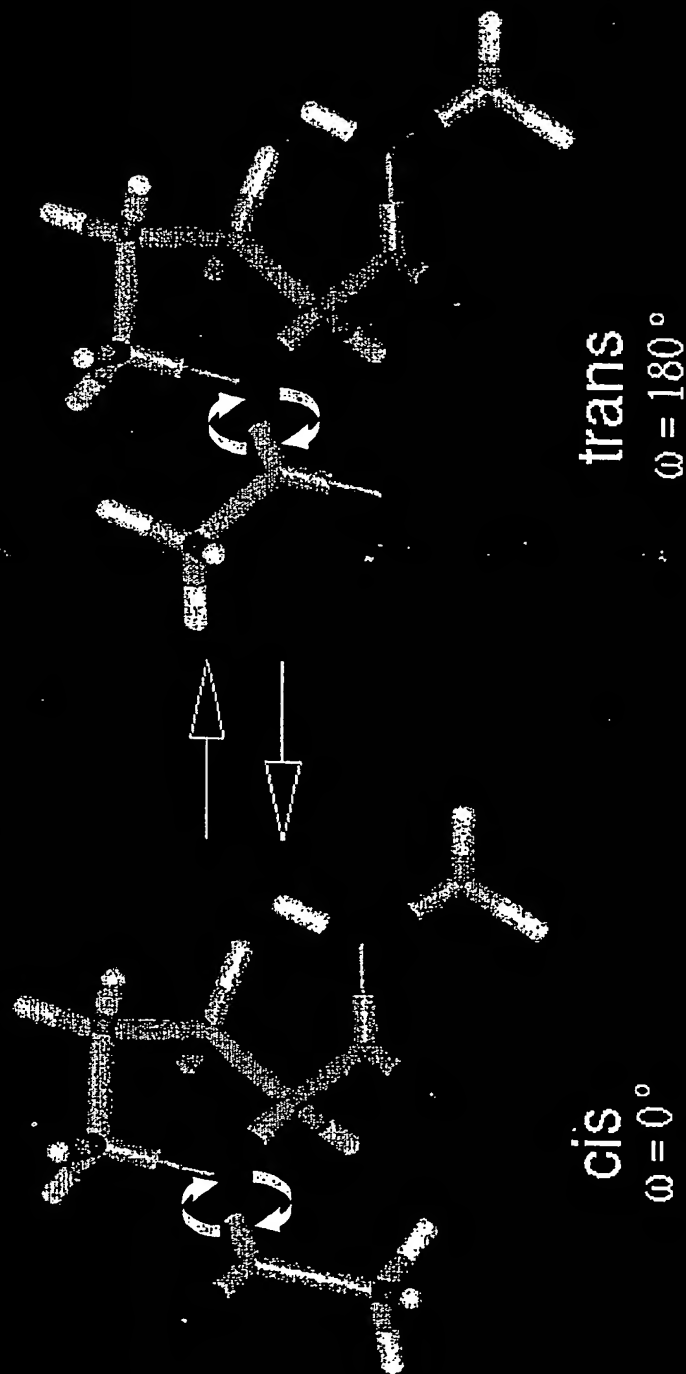
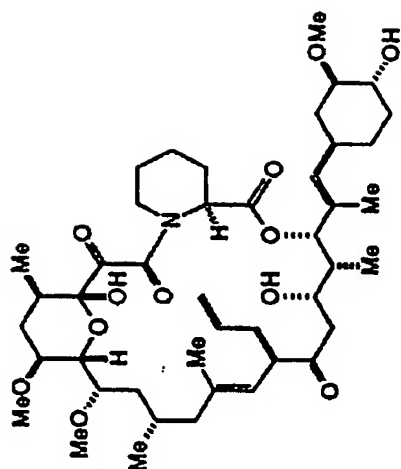
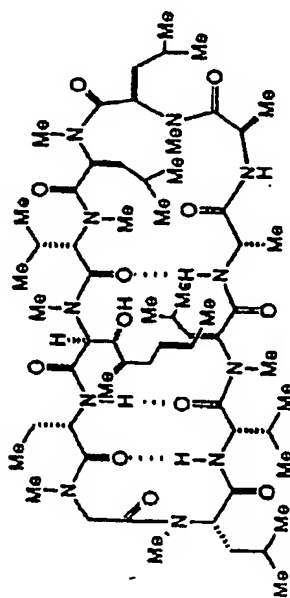


FIGURE 2

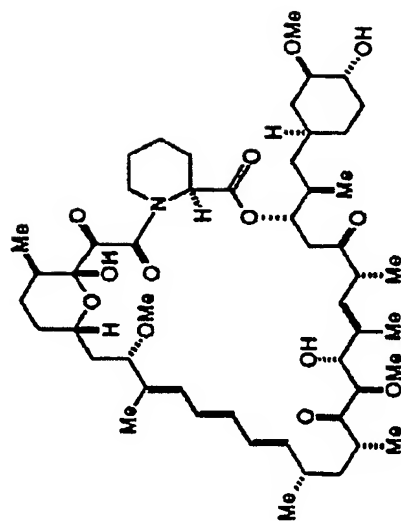
# Structure of Immunophilin Ligands



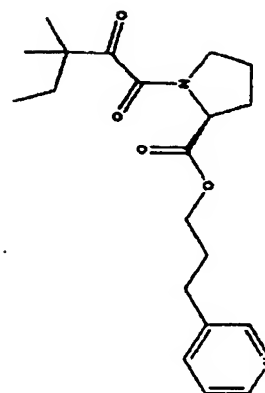
FK506



Cyclosporin A



Rapamycin



GPI-1046

FIGURE 3

# Effect of FK-506 on mGluR5 Binding to Homer

Time Course

mGluR5-transfected 293 Cells

1  $\mu$ M FK-506 Drug Time (in vivo)

0 15" 30" 1' 3' 6' 12' 24'

Homer3-GST

224 —

122 —

Offered

224 —

Buffer:

1 % TX-100

Calyculin A

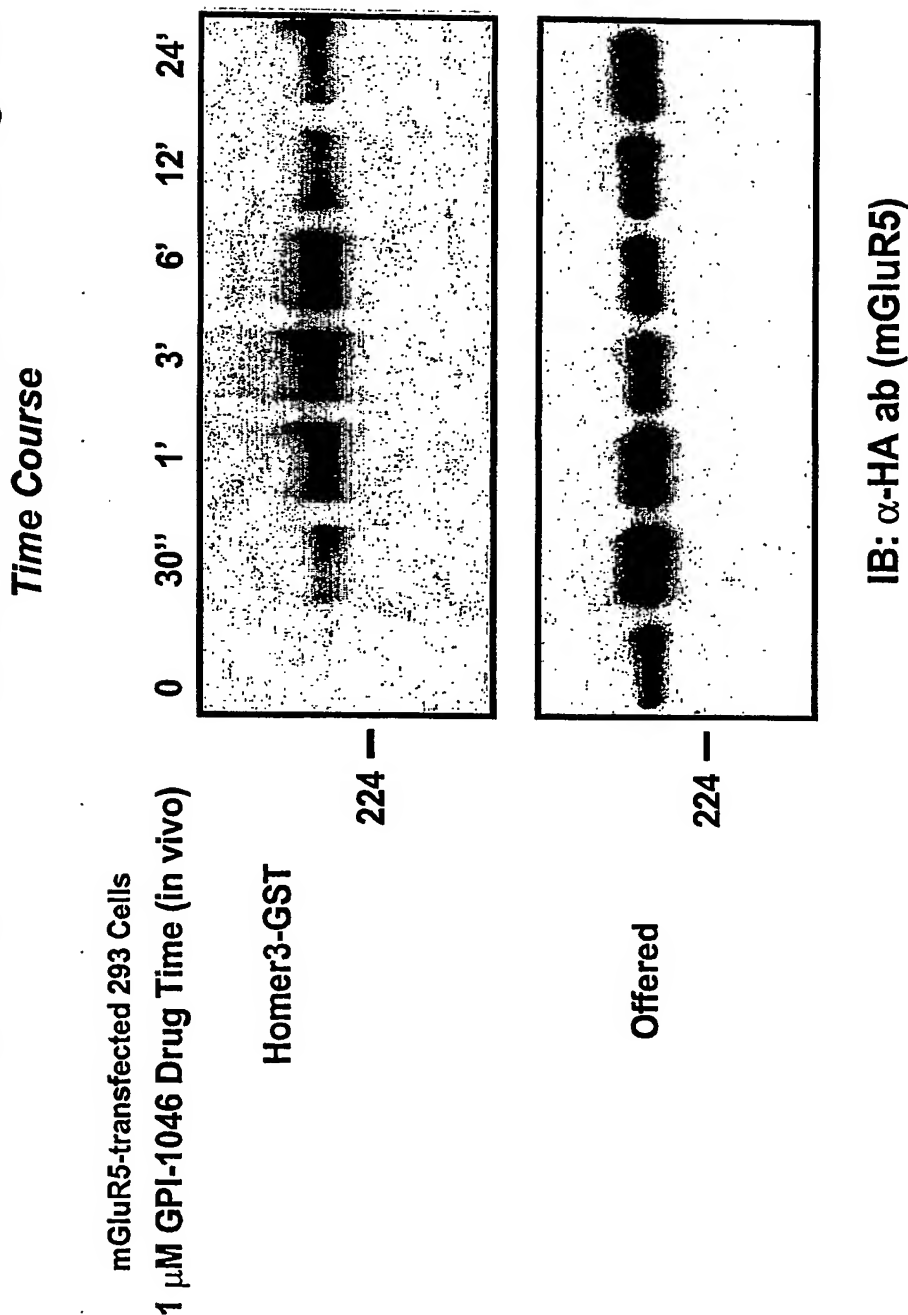
NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IB:  $\alpha$ -HA ab (mGluR5)

FIGURE 4

# Effect of GPI-1046 on mGluR5 Binding to Homer



**Buffer:**  
1 % TX-100  
Calyculin A  
NaF, NaPyrophosphate, NaVO3  
Protease Inhibitor

FIGURE 5

# FKBP52-GST Pulls Down mGluR5

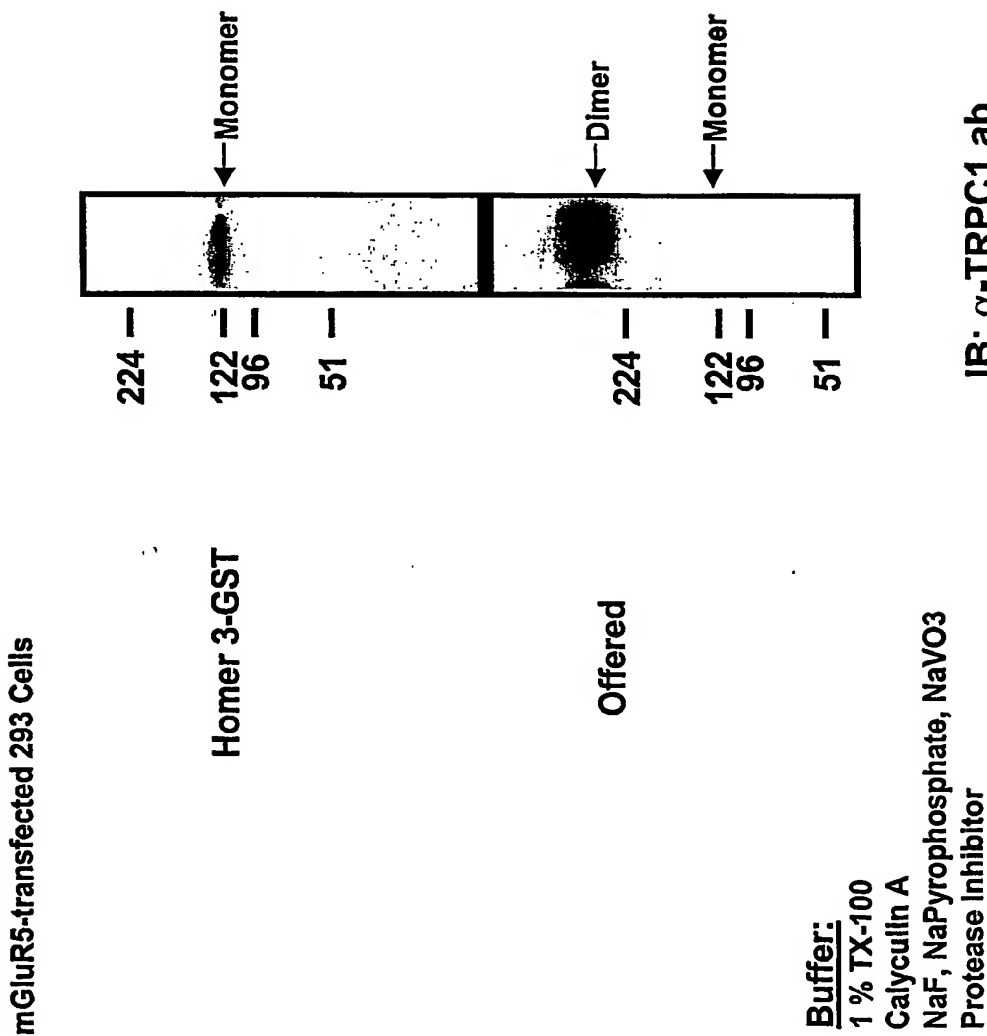
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# Increasing FKBP-12/-52 Increases Homer Binding to mGluR5

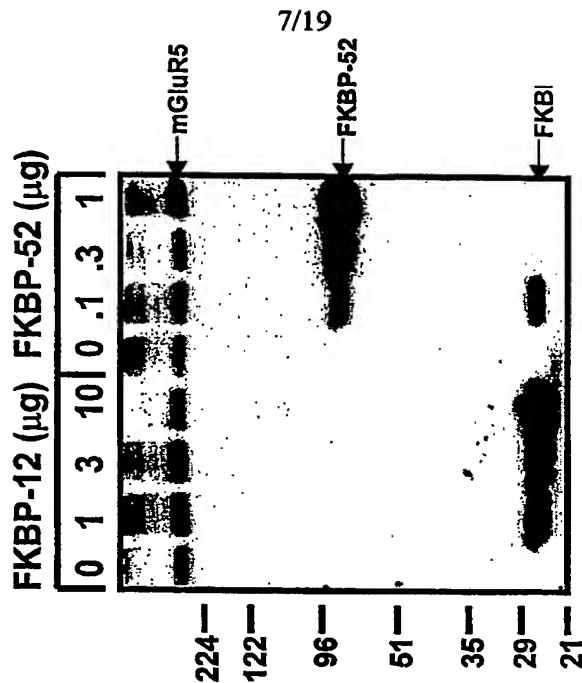
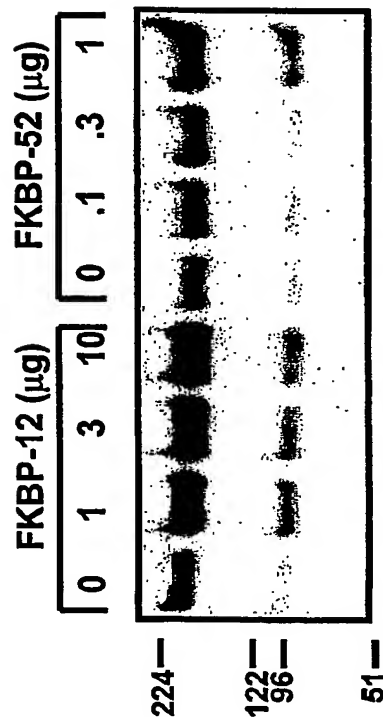
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10/518941

mGluR5-transfected 293 Cells +:



Buffer:

1 % TX-100

Calyculin A

NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IB:  $\alpha$ -HA ab

FIGURE 7

# Phylogenetic Relationship in the TRP Protein Family

Clapham et al., 2001

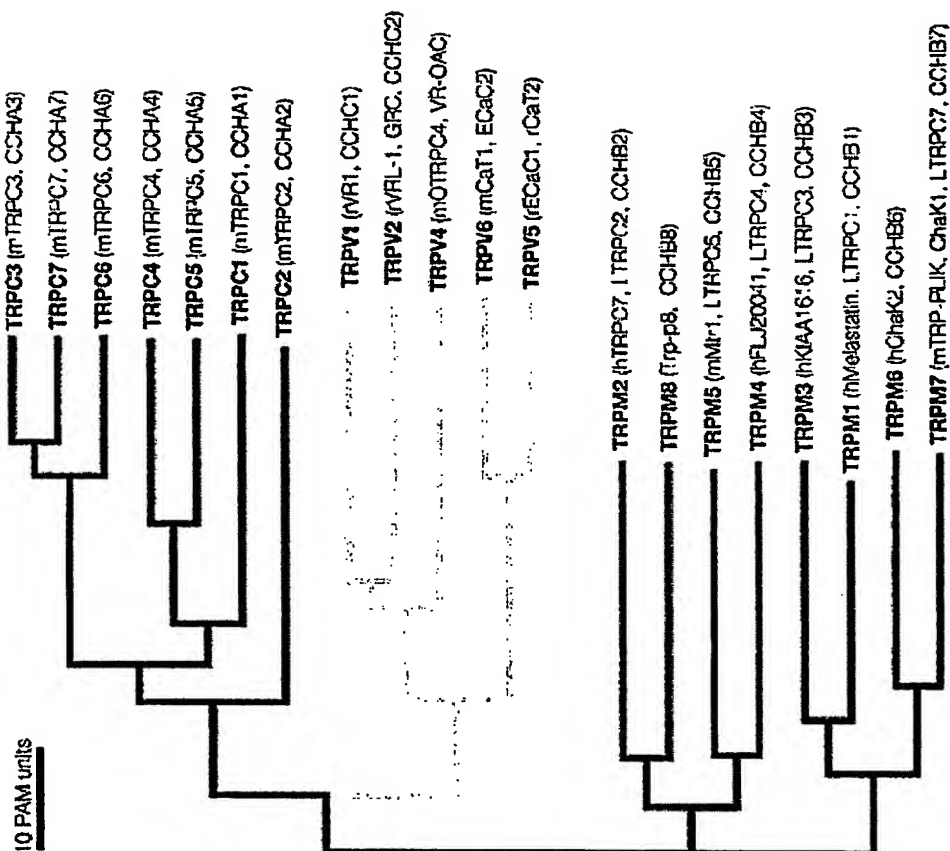
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FIGURE 8



# Amino Acid Sequence of TRPC1 and Alignment to Other TRP

Wes et al., 1995

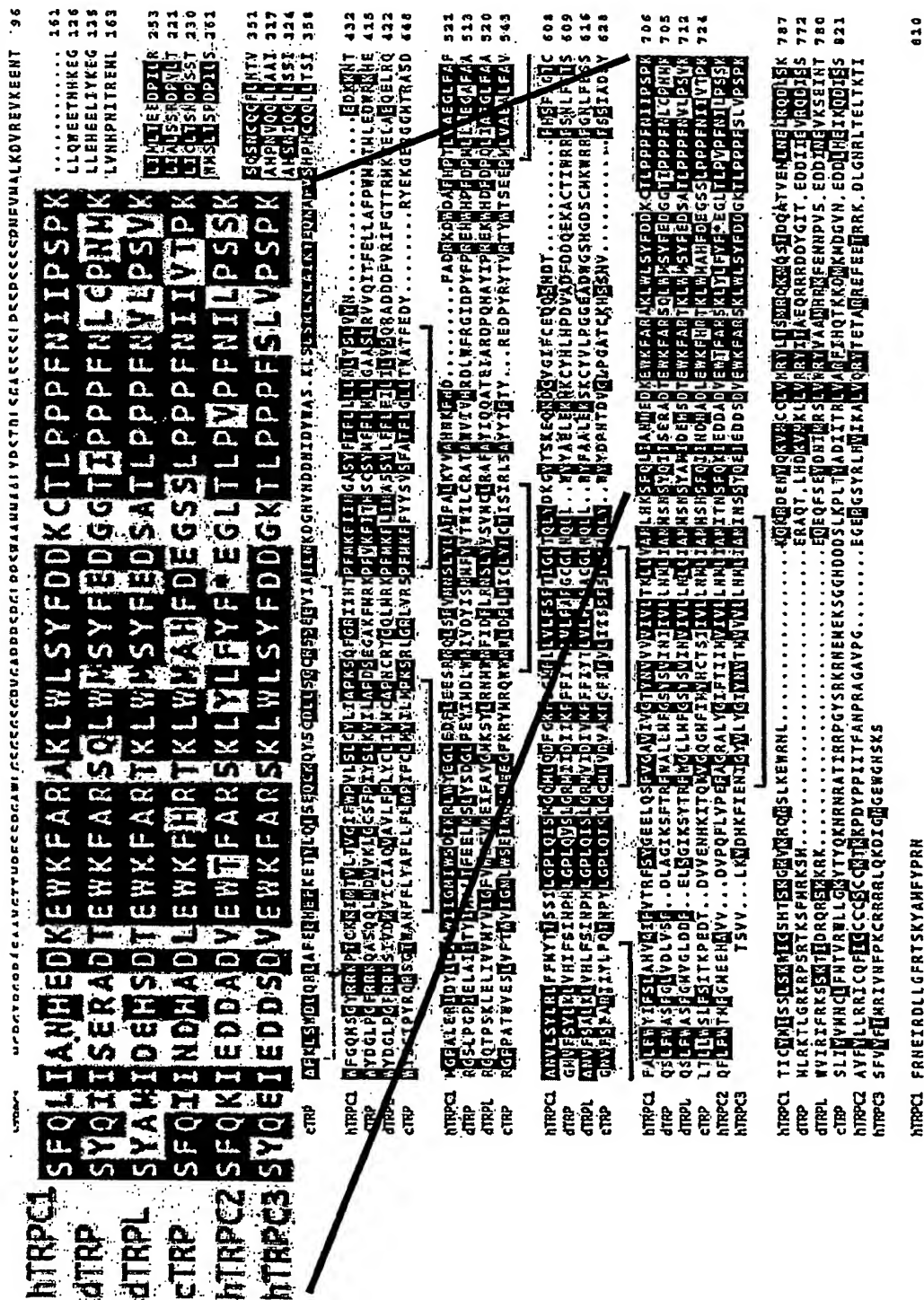
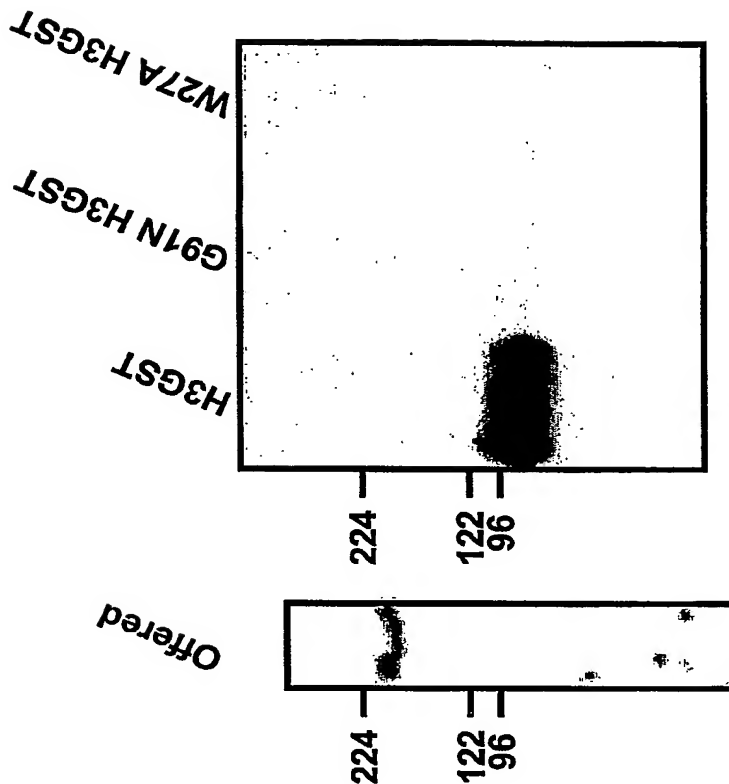


FIGURE 9

# Homer 3-GST Pulls Down TRPC1 from Cerebellum

Solubilized in 1 % TX-100  
 37,000 x g Spin



**Buffer:**  
 Calyculin A  
 NaF, NaPyrophosphate, NaVO3  
 Protease Inhibitor

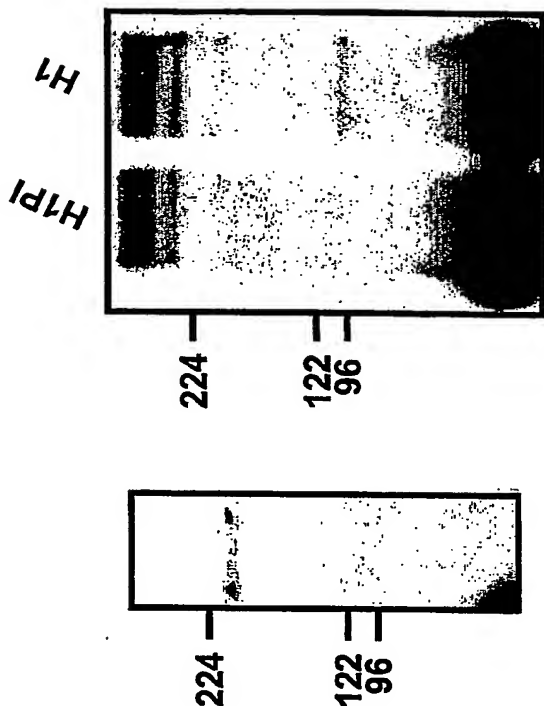
IB:  $\alpha$ -TRPC1 ab

FIGURE 10

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# Brain Co-IP of Homer and TRPC1

IP:  $\alpha$ -Homer 1 ab



**Hippocampus**

Buffer:

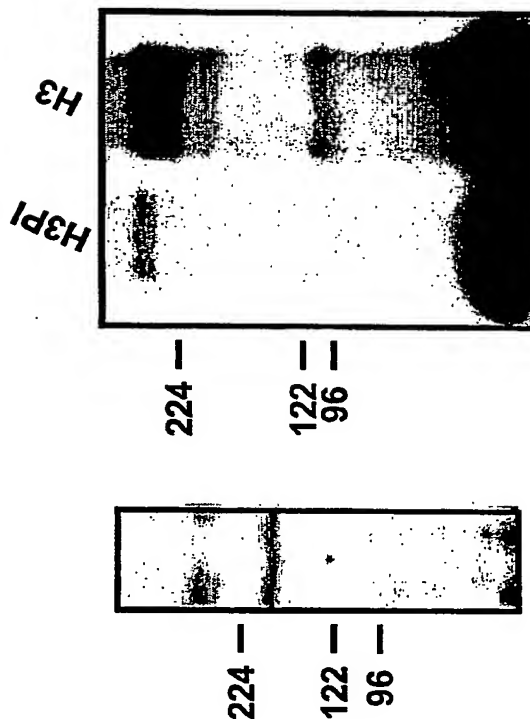
1 % TX-100

Calyculin A

NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IP:  $\alpha$ -Homer 3 ab



**Cerebellum**

Buffer:

1 % CHAPS

Calyculin A

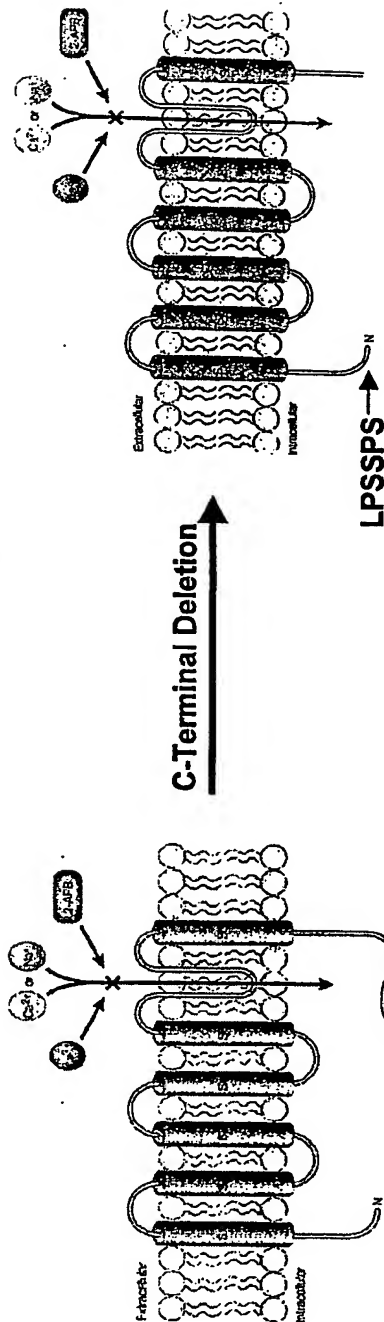
NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IB:  $\alpha$ -TRPC1 ab

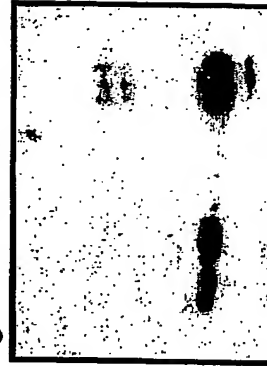
FIGURE 11

# Deletion of TRPC1 C-Terminus Reveals A Novel Homer Binding Site at the N-Terminus



GLUR1  
TRPC1 NT  
L19A  
P20A  
P23A  
P28A

Homer3-GS<sup>+</sup>

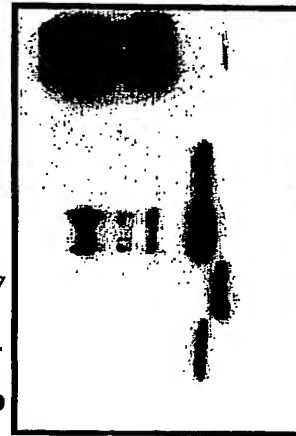


Offered

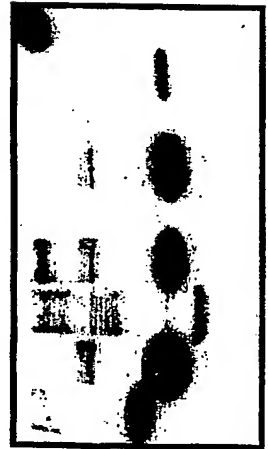


GLUR1  
TRPC1 wt  
Δ650-760  
P645L  
P646L  
F648R  
mgIUR5

Homer3-GST



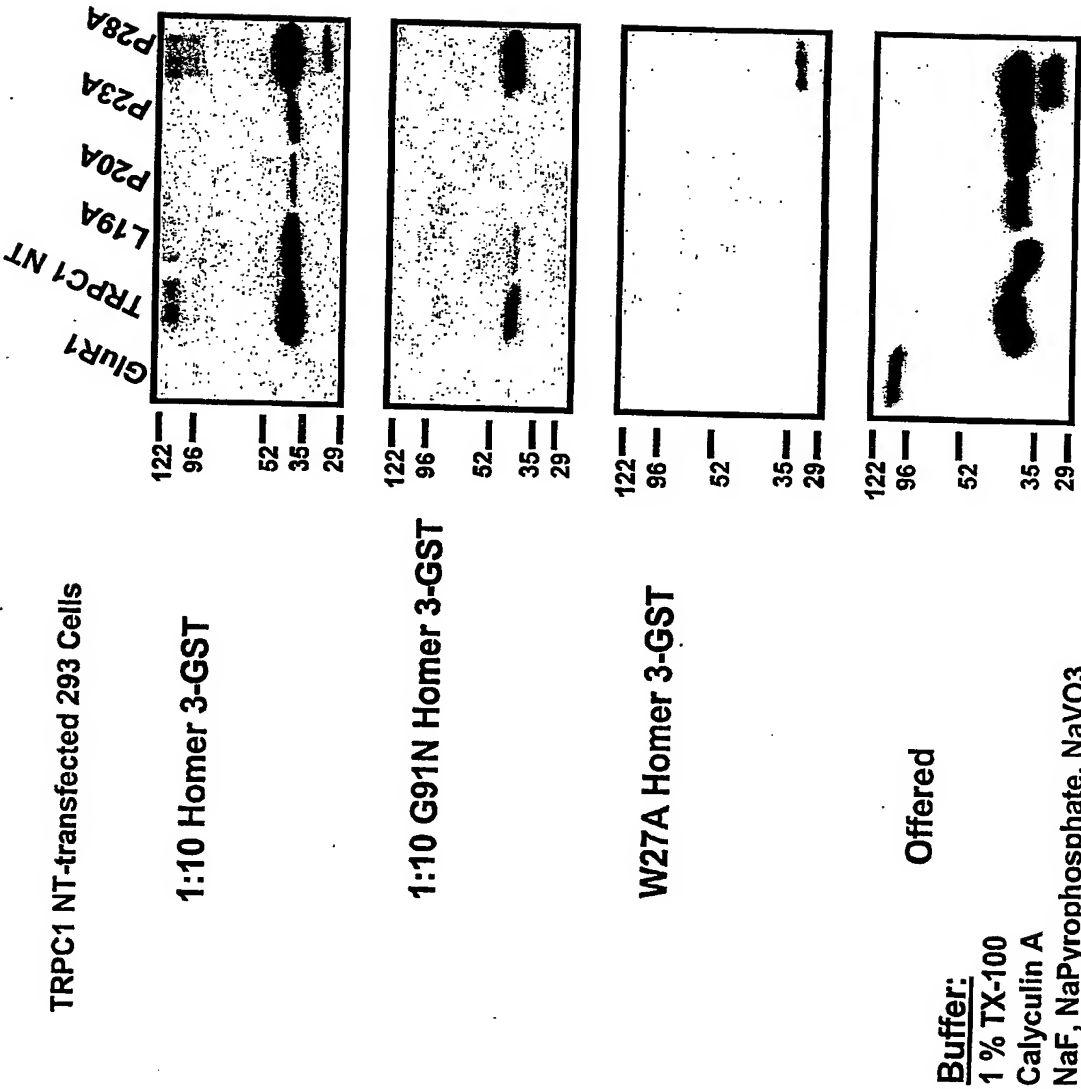
Offered



IB: α-HA ab (TRPC1)

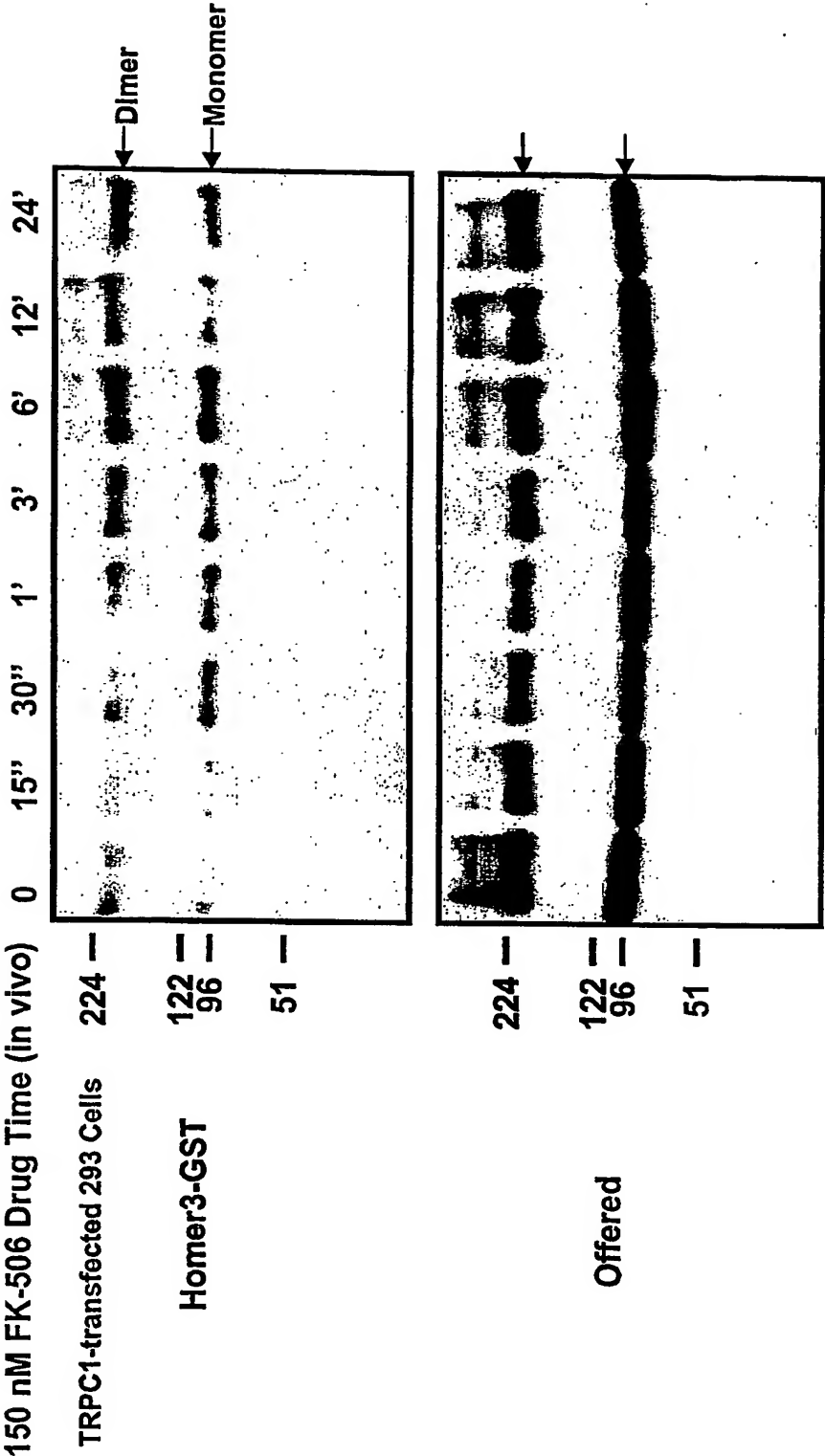
FIGURE 12

**WT and G91N Homer-GST Binds To  
LPSSP Motif of TRPC1 N-Terminus**



# Effect of FK-506 on TRPC1 Binding to Homer

Time Course



Buffer:  
1 % TX-100  
Calyculin A  
NaF, NaPyrophosphate, NaVO3  
Protease Inhibitor

FIGURE 14

# Effect of Various Drugs on TRPC1 Binding to FKBP52

## Dosage Dependence

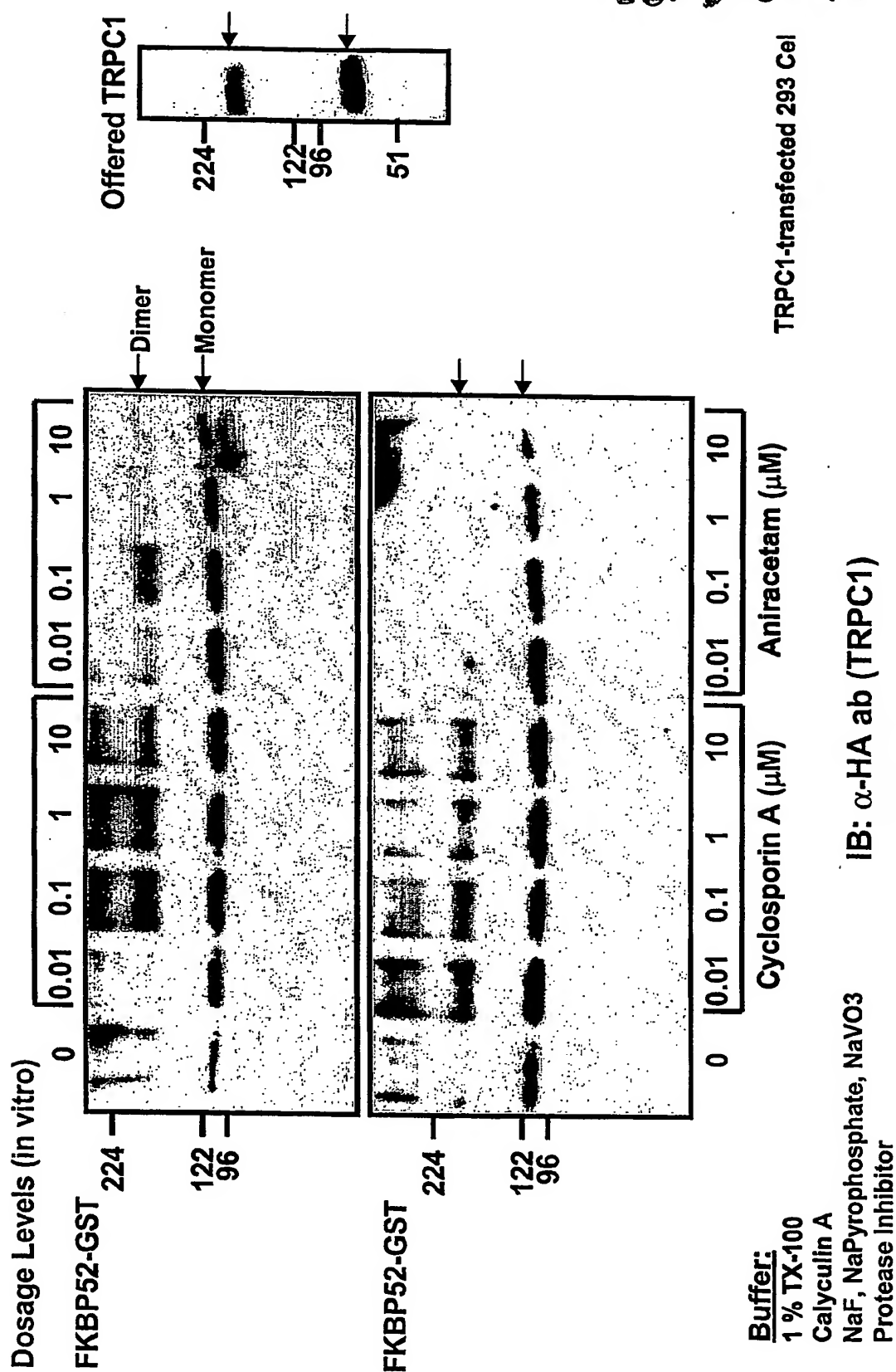


FIGURE 15

# Effect of FKBP-12/FKBP-52 on TRPC1 Binding to Homer

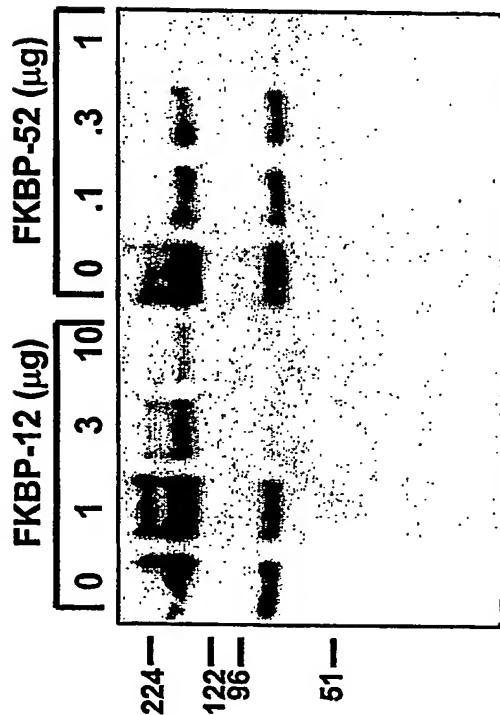
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TRPC1-transfected 293 Cells +:



Homer3-GST

Offered

Buffer:

1 % TX-100

Calyculin A

NaF, NaPyrophosphate, NaVO3

Protease Inhibitor

IB:  $\alpha$ -HA 3b (TRPC1)

FIGURE 16

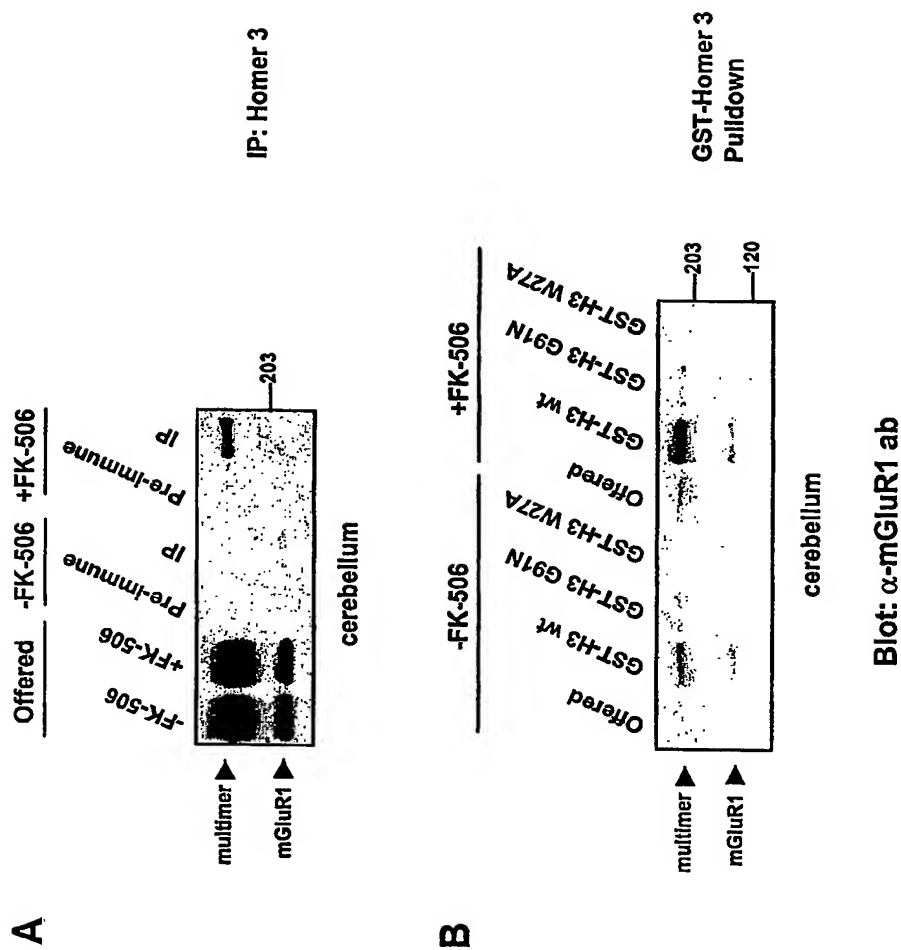


# Effect of FK-506 on Homer-mGluR1 interaction *in vivo*

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Adult rat was injected (i.p.) with 10 mg/kg FK-506 or vehicle only (DMSO). After 3 hours, the rats were sacrificed, and the cerebellum was collected. (A) Homer 3 co-immunoprecipitation of mGluR1 multimer increases with FK-506 treatment vs. control. (B) WT GST-Homer 3 pulldown of mGluR1 multimer increases with FK-506 treatment vs. control.

FIGURE 17

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atg ggg gaa caa cct atc ttc agc act cga gct cat gtc ttc cag atc  
gac cca aac aca aag aag aac tgg gta ccc acc agc aag cat gca gtt  
act gtg tct tat ttc tat gac agc aca agg aat gtg tat agg ata atc  
agt cta gac ggc tca aag gca ata ata aat agc acc atc act cca aac  
atg aca ttt act aaa aca tct caa aag ttt ggc caa tgg gct gat agc  
cgg gca aac act gtt tat gga ctg gga ttc tcc tct gag cat cat ctc  
tca aaa ttt gca gaa aag ttt cag gaa ttt aaa gaa gct gct cgg ctg  
gca aag gag aag tcg cag gag aag atg gaa ctg acc agt acc cct tca  
cag gaa tca gca gga gga gat ctt cag tct cct tta aca cca gaa agt  
atc aat ggg aca gat gat gag aga aca ccc gat gtg aca cag aac tca  
gag cca agg gct gag cca gct cag aat gca ttg cca ttt tca cat agg  
tac aca ttc aat tca gca atc atg att aaa

**Figure 18**

Met Gly Glu Gln Pro Ile Phe Ser Thr Arg Ala His Val Phe Gln Ile  
Asp Pro Asn Thr Lys Lys Asn Trp Val Pro Thr Ser Lys His Ala Val  
Thr Val Ser Tyr Phe Tyr Asp Ser Thr Arg Asn Val Tyr Arg Ile Ile  
Ser Leu Asp Gly Ser Lys Ala Ile Ile Asn Ser Thr Ile Thr Pro Asn  
Met Thr Phe Thr Lys Thr Ser Gln Lys Phe Gly Gln Trp Ala Asp Ser  
Arg Ala Asn Thr Val Tyr Gly Leu Gly Phe Ser Ser Glu His His Leu  
Ser Lys Phe Ala Glu Lys Phe Gln Glu Phe Lys Glu Ala Ala Arg Leu  
Ala Lys Glu Lys Ser Gln Glu Lys Met Glu Leu Thr Ser Thr Pro Ser  
Gln Glu Ser Ala Gly Gly Asp Leu Gln Ser Pro Leu Thr Pro Glu Ser  
Ile Asn Gly Thr Asp Asp Glu Arg Thr Pro Asp Val Thr Gln Asn Ser  
Glu Pro Arg Ala Glu Pro Ala Gln Asn Ala Leu Pro Phe Ser His Arg  
Tyr Thr Phe Asn Ser Ala Ile Met Ile Lys

Figure 19

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